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MINOR SESQUITERPENES FROM *MAYTENUS CHUBUTENSIS*

ANTONIO G. GONZÁLEZ,* MERCEDES P. NUÑEZ, ANGEL G. RAVELO, JAVIER G. LUIS, IGNACIO A. JIMÉNEZ,

Centro de Productos Naturales Orgánicos Antonio González, Carretera La Esperanza 2, La Laguna, 38206 Tenerife, Canary Islands, Spain

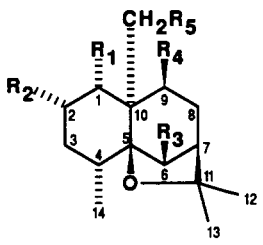
and ORLANDO M. MUÑOZ

Facultad de Ciencias, Universidad de Chile, Casilla 653, Santiago de Chile, Chile

ABSTRACT.—Four new minor dihydro-β-agarofuran-skeleton sesquiterpenes, 9β-benzoyloxy-1α,2α,6β-triacetoxy-15-hydroxydihydro-β-agarofuran [**1**], 9β-benzoyloxy-1α,2α,6β,15-tetracetoxydihydro-β-agarofuran [**6**], 9α-benzoyloxy-1α,2α,6β-triacetoxy-8α,15-dihydroxydihydro-β-agarofuran [**7**], and 9α-benzoyloxy-1α,2α,6β,8α-tetracetoxy-15-hydroxydihydro-β-agarofuran [**8**] were isolated from the aerial parts of *Maytenus chubutensis* and identified by spectroscopy and chemical reactions.

As part of an exhaustive program of research into secondary metabolites from species of Celastraceae used in folk medicine, we now report four new minor sesquiterpenes from *Maytenus chubutensis* Speg. (1), an Andean species from Chile. Six new sesquiterpenes (2) were earlier obtained from this plant as major compounds. All had the basic polyhydroxy skeleton of a pentahydroxydihydroagarofuran 6β-hydroxy derivative (3), and their absolute configurations were determined by cd. The compounds now isolated have two types of skeleton, the 3,4-dideoxymaytol type (4) and the alatol type (5).

Compound **1** had the molecular formula $C_{28}H_{36}O_{10}$, and ms fragments at *m/z* 105 and $[M-60]^+$ and $[M-42]^+$ suggested the presence of benzoate and acetate groups in the molecule. In the ^{1}H-nmr spectrum, signals for five aromatic protons appeared between δ 8.03 and 7.46, and the ^{13}C-nmr spectrum showed six aromatic carbons at δ 128.40 (×2), 129.60, 130.30 (×2) and 133.40. Signals were observed for three acetate methyls, at δ 2.10, 2.03, and 1.54 in the ^{1}H-nmr spectrum and at δ 20.52, 21.48, and 21.56 in the ^{13}C-nmr spectrum. The methyl signal at δ 1.54 indicated that an acetate and a benzoate group were facing each other at C-1 and C-9, or vice versa (6). An AB doublet centered at δ 4.29 and its carbon at δ 63.0 indicated the presence of a hydroxy-methylene grouping. This was confirmed by the OH bands seen in the ir spectrum and acetylation of **1**, which gave compound **6** with an extra acetate group and an AB doublet at δ 4.70. A three-proton doublet at δ 1.23 indicated the presence of a CH-Me group in the molecule. All the above data characterized **1** as a polyester sesquiterpene with a β-dihydroagarofuran skeleton.



1 R_1=R_2=R_3=OAc, R_4=OBz, R_5=OH
2 R_1=R_3=OAc, R_2=R_5=OH, R_4=OBz
3 R_1=R_2=OH, R_3=R_5=OAc, R_4=OBz
4 R_1=R_3=R_5=OH, R_2=OAc, R_4=OBz
5 R_1=R_2=R_5=OH, R_3=OAc, R_4=OBz
6 R_1=R_2=R_3=R_5=OAc, R_4=OBz

Double resonance experiments and the study of the coupling constants (Table 1) (4,7) gave the substitution positions as 1α,2α,6β,9β, and 15 with the customary (8) Celastraceae stereochemistry, as shown. The major products (2) isolated from the same species had the same stereochemistry. The ben-

TABLE 1. ^{1}H-nmr Spectra of Compounds **1–10**.[a]

Proton	Compound									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
H-1	5.66 d[b]	5.63 d[b]	4.60 d (3.6)	4.75 d (3.6)	4.50 d (3.6)	5.71 d (3.6)	5.51 d[b] (3.3)	5.51 d[b] (3.3)	5.57 d[b] (3.3)	5.54 d[b] (3.3)
H-2	5.53 m	4.43 m	4.15 m	5.42 m	4.21 m	5.62 m	5.31 m	5.34 m	5.37 m	5.39 m
H-3	1.79 dd (2.8, 14.0)				1.87 dd (2.8, 14.0)	1.80 dd (2.8, 14.0)	1.75 dd (2.5, 12.5)	1.75 dd 2.5, 12.5)	1.79 dd (2.5, 12.5)	
H-6	6.04 s	5.97 s	5.91 s	5.60 s	5.35 s	5.97 s	6.61 s	6.53 s	6.55 s	6.74 s
H-7	2.40 br d (6.0)	2.25 d[b]	2.28 d[b]	2.32[b]		2.47 d (5.0)	2.46 d (3.8)	2.62 d (4.0)	2.45 d (3.8)	2.45 d (3.6)
H-8							4.45 dd (3.8, 6.0)	5.51 dd[b] (4.0, 6.2)	4.45 dd (3.8, 6.0)	5.59 m[b]
H-9	5.67 d[b]	5.63 d[b]	5.40 d (7.0)	5.87 d (7.0)	5.76 d (7.0)	5.40 d (7.5)	5.54 d (6.0)	5.64 d (6.2)	5.56 d (6.0)	5.59 m[b]
H-15	4.23–4.33 d_{AB} (11.8)	4.34 d (5.0)	4.48–4.95 d_{AB} (13.6)	3.80–4.64 d_{AB} (13.6)	3.83–4.72 d_{AB} (13.6)	4.35–5.05 d_{AB} (13.5)	4.27–4.69 d_{AB} (12.0)	4.22 d–4.37 t (12.0)(12.0)	4.70–5.20 d_{AB} (12.0)	4.86–5.10 d_{AB} (12.0)
OAc	2.10, 2.03, 1.54	2.10, 1.63	2.08, 2.05	2.08	2.10	2.25, 2.11, 2.08, 1.54	2.08, 2.05, 1.47	2.10, 2.08, 2.05, 1.47	2.31, 2.12, 2.10, 1.48	2.30, 2.12, 2.10, 2.07, 1.48

[a]Spectra taken at 200 MHz in $CDCl_3$; chemical shifts in ppm from TMS; coupling constants in Hertz.
[b]Overlapping signals, with the most likely shown.

zoate could be assigned either to 1α or 9β, so **1** was hydrolyzed with 0.1 M $NaHCO_3$ at 50° to give products **2**, **3** (unexpectedly obtained by transacetylation), **4**, and **5**. The spectral data of these compounds (Table 1) led to the firm assignment of the benzoate group to 9β, and the structure of **1** was thus determined as 9β-benzoyloxy-1α,2α,6β-triacetoxy-15-hydroxydihydro-β-agarofuran with the basic polyhydroxy skelton of 3,4-dideoxymaytol (4). This skeleton is also found in compounds isolated from *Maytenus myrsinoides* Reiss which grows in Guyana and northeastern Brazil. As noted earlier, acetylation of **1** gave an acetate **6**. This was identical with one of the other sesquiterpenes isolated from *M. chubutensis*, and its structure was thus determined as 9β-benzoyloxy-1α,2α,6β,15-tetracetoxydihydro-β-agarofuran.

The other two natural products **7** and **8** were interrelated, as acetylation of **7** at room temperature afforded **8** and **9** while if **7** was heated to 60°, it gave **10**, also obtained by the acetylation of **8** for 60 h at room temperature. The ^{1}H-nmr data of all these products clearly indicated an alatol type of skelton (5) (Table 1). As the coupling constants J_{8-9} were similar for 8α,9α (9,10) and 8β,9β (11), the stereochemistry was confirmed by an nOe difference experiment on **7** whereby the irradiation of Me-12 affected the H-8β and H-9β (Figure 1). The ^{1}H-nmr spectra of the natural products **7** and **8** showed a signal for an acetate methyl at δ 1.47, which pointed to the benzoate being at C-1 or C-9 (6).

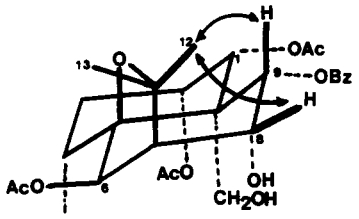


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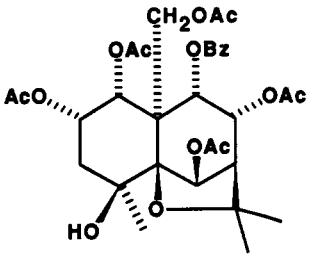
FIGURE 1. Results of an nOe difference experiment for compound **7**.

There was not enough sample for a selective hydrolysis, but the insect antifeedant celangulin [**11**], recently isolated from *Celastrus angulatus* (12), must be the 4β-hydroxyderivative of **10**. The ^{1}H-nmr spectra of celangulin and compound **10** were practically superimposable with the exception of the presence of a methyl doublet in **10** while all the methyls in celangulin appeared as singlets. The mass spectrum of celangulin showed fragments at *m/z* 261 and 202, which were also present in products **8** and **10**. In view of the foregoing, **7** must be 9-benzoyloxy-1α,2α,6β-triacetoxy-8α,15-dihydroxydihydro-β-agaro-furan and **8** must be 9α-benzoyl-



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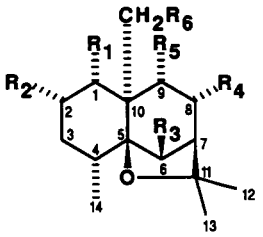

7 $R_1=R_2=R_3=OAc$, $R_4=R_6=OH$, $R_5=OBz$
8 $R_1=R_2=R_3=R_4=OAc$, $R_5=OBz$, $R_6=OH$
9 $R_1=R_2=R_3=R_6=OAc$, $R_4=OH$, $R_5=OBz$
10 $R_1=R_2=R_3=R_4=R_6=OAc$, $R_5=OBz$

oxy-1α,2α,6β,8α-tetracetoxy-15-hydroxydihydro-β-agarofuran.

EXPERIMENTAL

Ir spectra were taken on a PE 681 spectrophotometer and ^{1}H and ^{13}C nmr in $CDCl_3$ on a Bruker WP-200 SY (200 and 50 MHz, respectively) with TMS as internal reference. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Ms were recorded on a VG Micromass LTD-ZAB-2F and/or on an HP 5930A at 70 eV. Uv spectra were collected on a Perkin-Elmer model 550-SE.

PLANT COLLECTION.—The plant was gathered in January 1987, in the Septima region in Talca province, Chile, and a voucher specimen is lodged with the Facultad de Ciencias, Universidad de Chile, Santiago.

EXTRACTION AND ISOLATION.—The aerial parts of the plant were treated with EtOH to yield 44 g of extract. After repeated chromatography on Si gel with C_6H_{14}/EtOAc mixtures of increasing polarity as eluents, the following products were isolated: **1** (43 mg), **6** (5 mg), **7** (23 mg), and **8** (17.4 mg).

Compound **1** was isolated as a gum: $[\alpha]^{20}D$ 29.2° (c = 2.24, $CHCl_3$); ir ν max ($CHCl_3$) cm^{-1} 3000, 1730, 1360, 1275, 1240, 1080, 710; ^{1}H nmr δ 1.23 (3H, d, J = 7.6 Hz, Me-14), 1.40 (3H, s, Me-13), 1.44 (3H, s, Me-12), 7.46 (3H, m), 8.03 (2H, m), see Table 1 for additional data; ^{13}C nmr see Table 2; uv λ max (EtOH) nm 233, 276, 286; ms *m/z* (%) $[M]^+$ 532 (1), 517 (2), 490 (4), 430 (5), 472 (1), 410 (3), 365 (5), 350 (3), 308 (4), 105 (100); calcd for $C_{28}H_{36}O_{10}$, 532.2260, found 532.2284.

Hydrolysis of **1** (37 mg) with 0.1 M $NaHCO_3$ at 50° gave products **2** (2.8 mg), **3** (1.2 mg), **4** (3.7 mg), and **5** (5.4 mg).

TABLE 2. ^{13}C-nmr Data for Compound **1** (50 MHz, $CDCl_3$ as solvent).[a]

Carbon		Carbon	
C-1	72.48	C-12	18.15
C-2	69.31[b]	C-13	26.21
C-3	34.50	C-14	30.59
C-4	33.48	C-15	31.10
C-5	89.67	Acetate Methyls	20.52
C-6	70.17[b]		21.48
C-7	48.92		21.56
C-8	31.10	Acetate Carboxyls	170.13
C-9	78.90		170.01
C-10	55.13		169.19
C-11	82.62	Benzoate Carboxyls	165.63

[a]δ values based on DEPT experiments and correlations.

[b]Interchangeable values, most probably as shown.

Compound **2** was isolated as a thick oil: ir ν max ($CHCl_3$) cm^{-1} 3660, 3590, 3000, 2920, 2840, 1720, 1270, 1235, 1090, 710; ^{1}H nmr δ 0.93 (3H, d, J = 8.0 Hz, Me-14), 1.27 (3H, s, Me-13), 1.30 (3H, s, Me-12), 7.45 (3H, m), 8.05 (2H, m), see Table 1 for additional data; uv λ max (EtOH) nm 232, 274, 284; ms *m/z* (%) $[M]^+$ 490 (2), 448 (3), 430 (2), 385 (2), 368 (4), 326 (2), 323 (5), 308 (3), 290 (2), 105 (100); calcd for $C_{26}H_{34}O_9$, 490.2170, found 490.2186.

Compound **3** was isolated as a gum: ir ν max ($CHCl_3$) cm^{-1} 3660, 3580, 3000, 2920, 2840, 1720, 1360, 1270, 1235, 1090, 710; ^{1}H nmr δ 1.09 (3H, d, J = 7.5 Hz, Me-14), 1.42 (3H, s, Me-13), 1.50 (3H, s, Me-12), 7.48 (3H, m), 8.06 (2H, m), see Table 1 for additional data; uv λ max (EtOH) nm 230, 275, 284; ms *m/z* (%) $[M]^+$ 490 (19), 448 (94), 430 (32), 416 (28), 368 (36), 334 (38), 308 (33), 248 (16), 105 (100); calcd for $C_{26}H_{34}O_9$, 490.2170, found 490.2186.

Compound **4** was isolated as an oil: ir ν max ($CHCl_3$) cm^{-1} 3630, 3540, 3430, 3000, 2910, 2840, 1720, 1360, 1270, 1240, 1090, 710; ^{1}H nmr δ 1.14 (3H, d, J = 8.0 Hz, Me-14), 1.38 (3H, s, Me-13), 1.42 (3H, s, Me-12), 7.47 (3H, m), 8.05 (2H, m), see Table 1 for additional data; uv λ max (EtOH) nm 232, 276, 285; ms *m/z* (%) $[M]^+$ 448 (2), 430 (2), 385 (2), 368 (4), 323 (17), 248 (6), 203 (13), 105 (100); calcd for $C_{24}H_{32}O_8$, 448.2147, found 448.2122.

Compound **5** was isolated as a thick oil: ir ν max ($CHCl_3$) cm^{-1} 3690, 3420, 3020, 2920, 2840, 1720, 1360, 1275, 1240, 1090, 710; ^{1}H nmr δ 1.22 (3H, d, J = 7.6 Hz, Me-14), 1.40 (3H, s, Me-13), 1.48 (3H, s, Me-12), 7.49 (3H, m), 8.05 (2H, m), see Table 1 for additional data; uv λ max (EtOH) nm 274, 283; ms *m/z* (%) $[M-15]^+$ 433 (1), 338 (1), 326 (1), 308 (2), 281 (4), 248 (2), 105 (100); calcd for $C_{24}H_{32}O_8$, 448.2083, found 448.2090.

ACETYLATION OF **1**.—Product **1** (9 mg) was acetylated in the usual way (Ac_2O and pyridine) at room temperature giving a product identical to **6**.

Compound **6** was isolated as an oil (5 mg): $[\alpha]^{20}D$ 38.5° (c = 1.16, $CHCl_3$); ir ν max ($CHCl_3$) cm^{-1} 3000, 2920, 1720, 1360, 1275, 1240, 1065, 710; ^{1}H nmr δ 1.19 (3H, d, J = 7.6 Hz, Me-14), 1.42 (3H, s, Me-13), 1.45 (3H, s, Me-12), 7.50 (3H, m), 8.02 (2H, m), see Table 1 for additional data; uv λ max (EtOH) nm 232, 274, 286; ms *m/z* (%) $[M]^+$ 574 (1), 559 (15), 532 (57), 472 (2), 457 (1), 439 (1), 430 (1), 410 (6), 379 (1), 105 (100); calcd for $C_{29}H_{35}O_{11}$ $[M-15]^+$ 559.2127, found 559.2153.

Compound **7** was isolated as an oil (23 mg): $[\alpha]^{20}D$ −11.2° (c = 0.83, $CHCl_3$); ir ν max ($CHCl_3$) cm^{-1} 3590, 3440, 3000, 2920, 2840, 1730, 1360, 1265, 1235, 1085, 710; ^{1}H nmr δ

1.28 (3H, d, J = 7.7 Hz, Me-14), 1.40 (3H, s, Me-13), 1.50 (3H, s, Me-12), 7.45 (3H, m), 8.08 (2H, m), see Table 1 for additional data; ms *m/z* (%) $[M-60]^+$ 488 (3), 446 (1), 430 (2), 370 (3), 366 (4), 355 (2), 335 (4), 306 (4), 105 (100); calcd for $C_{28}H_{36}O_{11}$, 548.2157, found 548.2207.

Acetylation of **7** (9 mg) gave **8** (1.4 mg) and **9** (1 mg).

Compound **8** was obtained naturally as an oil (17.4 mg): ir ν max ($CHCl_3$) cm^{-1} 3565, 3020, 2920, 2840, 1735, 1365, 1270, 1230, 1090, 710; ^1H nmr δ 1.34 (3H, d, J = 7.5 Hz, Me-14), 1.39 (3H, s, Me-13), 1.54 (3H, s, Me-12), 7.51 (3H, m), 8.00 (2H, m), see Table 1 for additional data; ms *m/z* (%) $[M]^+$ 590 (2), 548 (2), 530 (4), 488 (2), 485 (1), 468 (1), 428 (2), 408 (2), 348 (3), 306 (6), 261 (2), 202 (3), 105 (100); calcd for $C_{30}H_{38}O_{12}$, 590.2395, found 590.2379.

Compound **9** was isolated as an oil: $[\alpha]^{20}D$ $-7.0°$ (c = 0.34, $CHCl_3$); ir ν max ($CHCl_3$) cm^{-1} 3580, 3000, 2910, 2840, 1735, 1365, 1270, 1225, 1090, 710; ^1H nmr δ 1.17 (3H, d, J = 7.5 Hz, Me-14), 1.45 (3H, s, Me-13), 1.52 (3H, s, Me-12), 7.51 (3H, m), 8.03 (2H, m), see Table 1 for additional data; ms *m/z* (%) $[M]^+$ 590 (1), 548 (16), 530 (2), 488 (7), 468 (2), 426 (2). 408 (7), 366 (3), 335 (7), 306 (3), 105 (100); calcd for $C_{30}H_{38}O_{12}$, 590.2417, found 590.2390.

ACETYLATION OF **7**.—Compound **7** (7 mg) was acetylated with Ac_2O and pyridine at 60° overnight and afforded **10** (7 mg) after chromatography.

Compound **10** was isolated as an oil: $[\alpha]^{20}D$ 2.3° (c = 0.60, $CHCl_3$); ir ν max ($CHCl_3$) cm^{-1} 3000, 2920, 2840, 1730, 1360, 1270, 1230, 1090, 710; ^1H nmr δ 1.17 (3H, d, J = 7.5 Hz, Me-14), 1.43 (3H, s, Me-13), 1.51 (3H, s, Me-12), 7.51 (3H, m), 8.01 (2H, m), see Table 1 for additional data; ms *m/z* (%) $[M]^+$ 632 (1), 590 (29), 572 (2), 548 (3), 530 (4), 488 (2), 457 (2), 412 (3), 370 (2), 366 (1), 306 (2), 261 (1), 202 (2), 105 (100); calcd for $C_{32}H_{40}O_{13}$, 632.2354, found 632.2411.

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